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EXAMINER

NGUYEN, B

ART UNIT

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8

DATE MAILED:

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This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

OFFICE ACTION SUMMARY

☒ Responsive to communication(s) filed on 11-20-96

☒ This action is FINAL.

☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) 1-10, 12-23, 25-34, 36-42, 44-49, 54-59, 61-67, 69-73, 75 & 78-96 are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) 1-10, 12-23, 25-34, 36-42, 44-49, 54-59, 61-67, 69-73, 75 & 78-96 are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of Reference Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

- SEE OFFICE ACTION ON THE FOLLOWING PAGES -

Part III DETAILED ACTION

1. Applicant's amendment filed November 26, 1996 have been received. Claims 11, 24, 35, 43, 50-53, 60, 68, 74, 76 and 77 have been canceled. Claims 78-96 have been added.

Claims 1-10, 12-23, 25-34, 36-42, 44-49, 54-59, 61-67, 69-73, 75 and 78-96 are pending.

2. The text of those US Codes not found in this office action can be found in the previous office action, paper no. 4.

Drawings

3. This application has been filed with informal drawings which are acceptable for examination purposes only. Formal drawings will be required when the application is allowed.

Claim Rejections - 35 USC § 112

4. Claims 49, 54-59, 61-69, 72, 73, 75, 81-90, 93 and 96 are rejected under 35 U.S.C. § 112, first paragraph, as the disclosure is enabling only for claims limited to the use of trehalose as the glass forming material. See M.P.E.P. §§ 706.03(n) and 706.03(z).

The specification discloses a method of incorporating a biological substance into foamed glass matrices by adding trehalose and a solvent specific for the substance to be stored, the substance itself, and at least one other additive, the additive can be an inhibitor of the Maillard reaction or volatile salts or volatile organic solvents. The volatile salts and solvents are used to enhance foam formation. The additive can also be a foam stabilizing agent

The specification teaches evaporating the solvent and subjecting the resulting syrup to a temperature and pressure sufficient to boil the syrup causing

bubbles to form, and removing the moisture thereby allowing the bubbles to form a glass-like material. The specification specifically teaches using trehalose, (alpha-D-Glucopyranoxyl-alpha-D-glucopyranoside), as the glass forming material. The specification also teaches choosing a solvent that is specific for the substance to be incorporated therein. The specification further teaches adjusting internal and external temperature and pressure so as to cause boiling of the syrup.

The specification does not teach modifying the carbohydrate either chemically or enzymatically.

The specification as disclosed is not enabled for all polyols or all natural, synthetic or modified carbohydrate as the glass forming material, as recited in the instant claims. It would require undue experimentation for one of ordinary skill in the art to determine if all polyols or all carbohydrates show similar stability values when used as a glass forming material. Furthermore, it has been demonstrated in the prior art that not all sugars are appropriate for use as glass forming material. In Trehalose Drying: A Novel Replacement for Freeze-Drying, 1991, pp. 47-53, Roser stated that reducing sugars should be avoided. Roser further stated in Table 1 of the same publication that tests on reducing and non-reducing sugar, with the exception of trehalose, show negative results for stability. In this publication, Roser also stated that any buffers used together with trehalose and the substance to be dried must be specific for the substance in order for the substance to retain its full activity when reconstituted. Roser also shows in a 1993 publication, A sweeter way to fresher food, that reducing sugars such as lactose and maltose do not confer the same stability as trehalose. Neither do disaccharide, sucrose, sugar alcohols, dextran as well as monosaccharide and monosaccharide alcohols.

Response to Arguments

5. Applicant's arguments filed 11/26/97 have been fully considered but they are not persuasive.

Applicant argues that the instant invention is not limited to stabilizing labile proteins but to making foamed glass matrices and the products derived therefrom, thus, requiring the specification to support a limitation not found in the claims is not sufficient to uphold a 35 USC 112, first paragraph rejection. This argument is not persuasive because the claims rejected under 35 USC 112, first paragraph, are specifically directed to methods of preserving biological substances in glass matrices and to the products derived therefrom. As such, only trehalose has been proven to be effective in the methods and products as claimed. No other sugars or carbohydrates have been demonstrated to have the same stability values and/or properties of trehalose.

Applicant argues that the references cited in support of the enablement rejection are mainly concerned with preserving the stability of the restriction enzyme *PstI*, which is notoriously unstable, therefore they do not apply to the instant invention because the instant invention is directed to storage of substances not as sensitive as *PstI*. This argument is not persuasive because the instant claims recite storage of biological substances in general, thus this recitation includes all those that may or may not be as sensitive as *PstI*, further, such recitation also includes those that may be more sensitive than *PstI*, in which case the claims are clearly not enabled. In addition, Applicant argues that the references cited do not make use of foamed glass matrices (FGM) which better enhance the stability of substances stored in them. This argument is not persuasive because although the method of the prior art is not the same as the method of the instant invention, both methods result in a glassy phase produced by sugars, therefore, the glassy state is an inherent property of sugars, observed when

the bulk of moisture is removed. Specifically, the article A sweeter way to fresher food teaches this glassy phase at pages 27-28.

Applicant argues that it is well within the skill of the ordinary artisan to modify carbohydrates using readily available material and according to knowledge in the art. Further, applicant argues that the ordinary artisan will readily appreciate the list of exemplary carbohydrates on page 8 of the specification which includes those obtained by reduction and by other chemical and enzymatic processes. This argument is not persuasive because the rejection is based on the fact that the specification does not teach how the carbohydrates are chemically or enzymically modified, as recited in claim 5. The list of carbohydrates compounds on page 8 is a list of compounds that have already been modified, and not a teaching of how the modification is performed.

6. Claims 1, 5, 9, 71-73, 75 and 80 are rejected under 35 U.S.C. § 112, second paragraph, as being vague and indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 5 is vague and indefinite because it is not clear as to what on the carbohydrate has been modified.

Claim 9 is vague and indefinite because it does not further limit the subject matter of claim 8 from which it depends, *i.e.* aqueous solvent and aqueous buffer solvent are seen to be the same.

Claim 71-73 and 75 are vague and indefinite with respect to the recitation of "obtainable" because it is unclear whether or not the FGM is obtained by the method of the claims. It is suggested that Applicant recites --obtained-- instead of obtainable to obviate the rejection.

Claim 80 is vague and indefinite with respect to the abbreviations "GPS" and "GPM". It is recommended that Applicant use the full name of these sugars.

Claim Rejections - 35 USC § 102

7. The rejection of claims 71 and 72 under 35 U.S.C. § 102(b) as being clearly anticipated by Wettlaufer et al (U.S. Patent No. 5,290,765) is withdrawn in view of Applicant's amendment to the claims.

8. Claims 1-4, 6, 8, 9, 13-18, 30-34, 36, 40, 41, 49, 54, 55, 62, 63, 71, 72, 78, 83, 84, 85, 90, 91 and 93 are rejected under 35 U.S.C. § 102(b) as being anticipated by Chivers (U.S. Patent No. 3,557,717) for reasons of record in the prior office action, paper no. 4.

Chivers teaches a method for making fine candy floss filaments from a molten liquid solution or syrup containing at least sugar and water (column 1, lines 2-5). Candy floss is a form of hard candy comprised of sugar in a noncrystalline, amorphous stated (column 4, lines 19-22). Chivers teaches mixing 85%-90% sucrose, 10%-15% water and flavoring or coloring ingredients, heating the solution to form a molten syrup, thereafter, boiling the syrup and removing the moisture so that the final content of the moisture is reduced to less than 1.5 percent (column 1, lines 48-54). Chivers teaches boiling the syrup at atmospheric pressure and high temperature ranging from 190°F to 300°F or even higher if desired (column 3, lines 35-75). Chivers also teaches adding butter to make caramel-flavored candy floss (column 5, line 30), molasses, salt and sodium bicarbonate (column 4, lines 37-40). These substances are added in an amount deemed appropriate for flavor and color.

Response to Arguments

9. Applicant's arguments filed 11/20/96 have been fully considered but they are not persuasive.

Applicant argues that the instant invention differs from Chivers because the instant invention teach FGM which is formed by obtaining a syrup, exposing the

syrup to condition that cause boiling or foaming and then allowing the composition to harden while still a foam. This argument is not persuasive because this is not recited in the claims under rejection, *i.e.* allowing the composition to harden while still a foam. The claim under rejection recites mixing a sugar with a solvent, exposing the mixture to a pressure and temperature to cause evaporation of the solvent and exposing the resulting syrup to pressure and temperature that causes FGM to form. This method is seen to be the same as the method taught by Chivers.

Claim Rejections - 35 USC § 103

10. Claims 10, 12, 19-23, 25-29, 42, 44-47, 57, 59, 61, 64-67, 69, 70, 73, 75, 81, 86, 87, 94 and 96 are rejected under 35 U.S.C. § 103 as being unpatentable over Chivers in view of Black (U.S. Patent No. 3,619,294), Samuels et al (U.S. Patent No. 5,422,384) and Wettlaufer (U.S. Patent No. 5,290,765) for reasons of record in the prior office action, paper no. 4.

See discussion of Chivers above. Chivers differs from the instant invention in failing to teach the use of volatile organic solvent, or varying the pressure to cause boiling of the syrup or boiling the syrup so that a glass-like substance is formed from the molten mixture. Chivers also did not teach adding medicinal agents to the solution nor reconstituting the final product in appropriate solvents.

Black teaches a method of combining sugar, organic and inorganic solvents and various additives to produce powdered-drinks or tablets. Black teaches the use of sugars such as sucrose, fructose, maltose, and lactose and a combination of organic or inorganic solvent (column 3, lines 59-60 and column 4, lines 1-8), evaporating the solvent to reduce the moisture content and when desired, reconstituting the final product with a suitable solvent. Black teaches the addition of volatile oils and guar gum as a coating material (column 6, lines 52 and 75). Black also teaches the addition of medicines, vaccine and other fruit or liquor

flavor such that when reconstituted can be used as drinks. Black also teaches that when a medicinal agent or vaccine is incorporated in the final product, it is present in a therapeutically appropriate amount (column 10, lines 7-10).

Samuels teaches a method of making a glass/polymer composite by mixing a glass making material with an appropriate solvent. Heating the solution to evaporate the solvent leaving a molecular mixture, gel or the like. And heating the mixture to produce a glass/polymer composite (column 4, lines 6-12). Samuels teaches a mixture of both inorganic and organic solvent such as alcohols and ethers (column 4, lines 14-20 and column 5, lines 38-40). Samuels also teaches elevating the temperature and pressure as desired. The temperature can be elevated to 40°C or 100°C (column 5, lines 11-14).

It would have been obvious for one of ordinary skill in the art at the time the invention was made to adjust the temperature and pressure, as taught by Samuels, in the method of Chivers to optimize the heating and evaporation procedure because Samuels shows it to be conventional in the art.

It would have been obvious to one of ordinary skill in art at the time the invention was made to use a mixture of organic and inorganic solvent such as taught by Black, because organic solvent aid in the dispersion of the additives or modifying agent (Black, column 4, lines 1-5).

It would have been obvious to one of ordinary skill in the art that the fine floss filament of Chivers is in a noncrystalline amorphous state, which, by definition, is a glossy glass-like material in the form of fine filaments. This form of glass-like product is obtained when most of the moisture is removed from the mixture. It is well known in the art that the ability to form a glassy solid state is indicative of soluble sugar under appropriate conditions (Wettlaufer, U.S. Patent No. 5,290,765).

In addition, it would have been obvious to one of ordinary skill in the art at the time the invention was made that various additives may be included in the mixture (Chivers, column 3, lines 5-10). One of ordinary skill would have had a reasonable expectation of success in using the medicinal agents and vaccine of Black in the method of Chivers because Black shows it to be well known and conventional in the art.

11. Claims 7, 80, 92 and 95 are rejected under 35 U.S.C. § 103 as being unpatentable over Chivers in view of Black, Samuels et al and Wettlaufer as applied to claims 1-4, 6, 8-10, 12-23, 25, 34, 36, 40-42, 44-47, 49, 54, 55, 57, 59, 61-67, 69-73, 75, 78, 81, 83-87, 90-91, 93, 94 and 96 above and further in view of Roser (GB 2,206,273).

See discussion of Chivers, Black, Samuels and Wettlaufer above. Chivers differs from the instant invention in failing to teach the use of trehalose as the sugar.

Roser teaches a similar invention whereby trehalose is used to preserve proteinaceous material. Roser teaches trehalose mixed with proteinaceous foodstuffs and heated to high temperatures, 40°C to 80°C, or 175°C to 205°C, or 85°C or 98°C (page 6). Roser also teaches that the resultant product can be reconstitute in appropriate solvent.

It would have been obvious for one of ordinary skill in the art at the time the invention was made to use the trehalose, as taught by Roser, in the method of Chivers because Roser shows that trehalose is more efficient than other sugars and does not render the product too sweet (page 4).

Response to Arguments

12. Applicant's arguments filed 11/26/96 have been fully considered but they are not persuasive.

In response to applicant's argument that the references are from non-analogous art, it has been held that a prior art reference must either be in the field of applicant's endeavor or, if not, then be reasonably pertinent to the particular problem with which the applicant was concerned, in order to be relied upon as a basis for rejection of the claimed invention. In this case, Applicant argues that Chivers is non-analogous because Chivers teach apparatus and methods for making candy floss, which is designed for immediate consumption and not for long-term storage. Further, an ordinary artisan would not be motivated to add small molecules of drugs and/or viral particles to candy floss. This argument is not persuasive because Chivers in view of Black is seen to render the instant claims obvious. Chivers teaches the use of various sugars incorporated with additives for consumption and Black teaches the use of the same or obvious variation of the same sugars for storage of medicinal and vaccine components also for consumption. The argument that the candy floss of Chivers is for immediate consumption, whereas the instant invention is for long term storage is not persuasive because this is not recited in the rejected claims.

Applicant argues that Samuels et al teach glass making methods and composition and thus is non-analogous art. This argument is not persuasive because the Samuels et al reference is used to teach evaporation of various solvents using increased temperature and pressure and not for the teachings of polymers used in glass making. Samuels et al show that it is conventional and well known in the art that increased temperature and pressure are routinely used to evaporate solvents from a mixture.

Applicant argues that Black et al is non-analogous art because Black et al teach impregnated microcrystalline sugar granules and since granules are crystalline, they are structurally distinct from the instant invention. This argument is not persuasive because Black et al teach the use of the same or obvious variation of the same sugars of the instant invention and of the Chivers reference, and Black et al also teach adding medicines, vaccine or other additives such as volatile oils and guar gum to the mixture, evaporating the solvent to obtain a product. The combination of Chivers and Black et al is seen to render the instant claims obvious. Further, the Black et al reference is not relied upon for the teachings of product structures, but is relied upon for the teachings of volatile organic solvents, viscosity agents and medicinal components.

Applicant argues that even if combined, the combination does not produce FGMS. This argument is not persuasive the references teach all of the reagents and steps involved in the instant method, therefore, it would have been obvious that when combined, the prior art method would produce the same or obvious variation of the same product of the instant invention.

Allowable Subject Matter

13. Claims 37-39, 48, 56, 58, 79, 82, 86, 88 and 89 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

14. No claim is allowed.

15. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

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A shortened statutory period for response to this final action is set to expire THREE MONTHS from the date of this action. In the event a first response is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event will the statutory period for response expire later than SIX MONTHS from the date of this final action.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bao-Thuy Nguyen whose telephone number is (703) 308-4243. The examiner can usually be reached Monday through Friday, from 7:30 AM to 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel, can be reached on (703) 308-4027. The fax phone number for this Group is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

BTN
March 3, 1997


CHRISTOPHER L. CHIN
PRIMARY EXAMINER
GROUP 1800